REMARKS

Claims 1-19 and 45-57 were pending in the application and subject to a restriction requirement. Specifically, the Office Action has identified the following groups:

I. Claims 1-8 and 11-19, drawn to a method for stimulating an immune response specific toward a naturally occurring protein in an animal having an immune system including T cells, said method comprising administering to said animal an altered protein derived from said naturally occurring protein, wherein an unstable polypeptide segment has been inserted by artifice into said altered protein, classified in Class 424, subclass 185.1,

II. Claims 9-19, drawn to method for increasing the immunogenicity of a naturally occurring protein, said method comprising inserting by artifice into said naturally occurring protein an unstable polypeptide segment to produce an altered protein, classified in Class 514, subclass 2,

III. Claims 45-57, drawn to a substantially pure antigen comprising an unstable polypeptide segment inserted by artifice, classified in Class 530, subclass 350.

Applicant has amended claim 9 to depend from claim 1, thus bringing claims 9 and 10 within the ambit of Group I. Support for the amendment of claim 9 is found throughout the application as filed, including, for example, page 2, lines 14-17; page 13, lines 17-18; page 27, lines 14-20, as well as claim 9 as originally filed. Applicant has also added claim 58 as a specific embodiment, in view of the species election requirement in the Office Action. Upon entry of the instant amendment, claims 1-19 and 58 will be pending in the application. For the examiner's convenience, a copy of all pending claims is enclosed with this Reply. No new matter has been added.

Applicant submits that, upon entry of the instant amendments, all pending claims will fall under Group I. Accordingly, Applicant respectfully requests reconsideration of the restriction requirement based on the amendment of claim 9.

The Office Action has also required a species election. In particular, the Office Action states that Applicant is required:

A. To elect a specific embodiment: of a specific altered protein, a specific alteration of a specific naturally occurring protein of a specific animal,

B. To elect a specific embodiment: of the rejected unstable polypeptide segment, wherein a specific number of amino acid residues are inserted in said unstable polypeptide segment as recited in claim, wherein said polypeptide sequence is recognized by a specific protease a cell-derived antigen, wherein said polypeptide sequence has one of the specific properties recited in claims 14, 18, 49, and 53 and wherein said altered protein comprises an epitope for a specific immune cell such as a T cell as recited in claim 15, (if T cell is selected then a specific type of T cell is requested IE T helper or T killer))

In response, Applicant makes the following elections:

Specific altered protein: **HIV gp120**

Specific alteration: **insertion of human Hsp 10 mobile loop**

Specific animal: **human**

Specific number of amino acid residues: **sixteen**

Specific protease recognition: **cathepsin S**

Specific property of claim 14: **an average hydrophobicity value that is lower than the average hydrophobicity value of said altered protein**

Specific property of claim 18: **an average hydrophobicity value that is higher than the average hydrophobicity value of said altered protein**

As further required by the Office Action, Applicant elects the specific embodiment of claim 58, if no generic claim is finally held to be allowable. Also,

Applicant submits that newly added claim 58, and all pending claims, read upon the elected embodiment.

Applicant notes that the forms PTO-1449 submitted with the Information Disclosure Statement filed July 11, 2000 have not been initialed and returned and hereby requests that they be initialed and returned with the next action.

If there are any charges, or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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Version with Markings to Show Changes Made

9. (Amended) [A] The method of claim 1, wherein [for increasing the] immunogenicity of [a] the naturally-occurring protein is increased.[, said method comprising inserting by artifice into said naturally-occurring protein an unstable polypeptide segment to produce an altered protein.]

58. (New) A method for stimulating an immune response toward a naturally occurring protein in a human, said method comprising administering to said human an altered HIV gp120 protein, wherein a human Hsp 10 mobile loop said has been inserted by artifice into said altered HIV gp 120 protein.

Pending Claims

1. A method for stimulating an immune response specific toward a naturally-occurring protein in an animal having an immune system including T cells, said method comprising administering to said animal an altered protein or polypeptide fragment thereof derived from said naturally-occurring protein, wherein an unstable polypeptide segment has been inserted by artifice into said altered protein.

2. The method of claim 1, wherein said naturally-occurring protein is from a pathogen.

3. The method of claim 2, wherein said altered protein or polypeptide fragment thereof is administered to said animal to prevent infection of said animal with said pathogen.

4. The method of claim 1, wherein said naturally-occurring protein is from a neoplastic cell,

5. The method of claim 4, wherein said altered protein or polypeptide fragment thereof is administered to said animal to inhibit growth of said neoplastic cell in said animal.

6. The method of claim 1, wherein said altered protein or polypeptide fragment thereof is administered with a pharmaceutically acceptable carrier, an adjuvant or both.

7. The method of claim 1, wherein said animal is a mammal.

8. The method of claim 7, wherein said mammal is a human.

9. The method of claim 1, wherein immunogenicity of the naturally-occurring protein is increased.

10. The method of claim 9, wherein said altered protein or polypeptide fragment thereof is in a vaccine.

11. The method of claim 1 or 9, wherein said unstable polypeptide segment comprises at least twelve amino acid residues.

12. The method of claim 11, wherein not more than 30% of said amino acid residues are selected from the group of amino acid residues consisting of isoleucine, leucine, valine, tyrosine, phenylalanine, tryptophan, threonine, and methionine.

13. The method of claim 1 or 9, wherein said unstable polypeptide segment comprises a polypeptide sequence that is specifically recognized by a protease.

14. The method of claim 1 or 9, wherein said unstable polypeptide segment has an average hydrophobicity value that is lower than the average hydrophobicity value of said altered protein; has a sequence conservation that is lower than a sequence conservation of said altered protein; has an amide protection factor that is lower than 10^4 wherein said altered protein is in a native conformational state; has an average amide protection factor that is lower than the average amide protection factor for said altered protein in a denatured conformational state; has an NMR order parameter (S^2) of less than 0.8; or has an average B-factor value that is higher than the average B-factor value of said altered protein.

15. The method of claim 1 or 9, wherein said altered protein comprises a T cell epitope.

16. The method of claim 15, wherein said unstable polypeptide segment is inserted N-terminally adjacent to said T cell epitope.

17. The method of claim 15, wherein the C - terminal portion of said unstable polypeptide segment overlaps the N - terminal portion of said T cell epitope.

18. The method of claim 15, wherein said T cell epitope has an average hydrophobicity value that is higher than the average hydrophobicity value of said altered protein; has a sequence conservation that is higher than a sequence conservation of said altered protein; has an amide protection factor that is greater than 10^4 wherein said altered protein is in a native conformational state; has an average amide protection factor that is higher than the average amide protection factor for said altered protein in a denatured conformational state; has an NMR order parameter (S^2) of greater than 0.7; or has an average B-factor value that is lower than the average B-factor value of said altered protein.

19. The method of claim 15, wherein at least 30% of the amino acid residues of said T cell epitope are selected from the group of amino acid residues consisting of isoleucine, leucine, valine, tyrosine, phenylalanine, tryptophan, threonine, and methionine.

58. A method for stimulating an immune response toward a naturally occurring protein in a human, said method comprising administering to said human an altered HIV gp120 protein, wherein a human Hsp 10 mobile loop said has been inserted by artifice into said altered HIV gp 120 protein.